

2. (Amended) A method for inhibiting an altered growth state of a cell having a ptc loss-of-function phenotype or a ~~smoothened~~ gain-of-function phenotype, comprising contacting the cell with a composition in a sufficient amount to inhibit the altered growth state, wherein the composition comprises a purified organic molecule having a molecular weight less than 750 amu and which interacts with ~~smoothened~~ or a complex comprising ~~smoothened~~ and inhibits aberrant signal transduction resulting from a ~~patched~~ loss-of-function or ~~smoothened~~ gain-of-function phenotype.

Sub
C2
15. (Amended) The method of any of claims 1-3, wherein the organic molecule inhibits hedgehog-mediated signal transduction with an ED₅₀ of 1 mM or less.

16. (Amended) The method of any of claims 1-3, wherein the organic molecule inhibits hedgehog-mediated signal transduction with an ED₅₀ of 1 μM or less.

B2
17. (Amended) The method of any of claims 1-3, wherein the organic molecule inhibits hedgehog-mediated signal transduction with an ED₅₀ of 1 nM or less.

18. (Amended) The method of claim 2, wherein the cell is contacted with the organic molecule *in vitro*.

19. (Amended) The method of claim 2, wherein the cell is contacted with the organic molecule *in vivo*.

Sub
C3
20. (Amended) The method of claim 1, wherein the organic molecule is administered as part of a therapeutic or cosmetic application.

21. (Amended) The method of claim 1, wherein the organic molecule is administered to treat a condition selected from regulation of neural tissues, bone and cartilage formation and repair, regulation of spermatogenesis, regulation of smooth muscle, regulation of lung, liver and other organs arising from the primitive gut, regulation of hematopoietic function, and regulation of skin and hair growth.

22. (Amended) The method of claim 1, wherein the organic molecule is administered [applied] as a topical formulation to skin to inhibit aberrant proliferation of epithelial cells.

23. (Amended) The method of claim 1, wherein the organic molecule is administered to the patient to inhibit growth of a basal cell carcinoma.

25. (Amended) A pharmaceutical preparation formulated for topical application, comprising a purified organic molecule having a molecular weight less than 750 amu, wherein the organic molecule interacts with *smoothened* or a complex comprising *smoothened* and lessens the severity of a *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function phenotype.

Please add the following new claims:

27. (New) A method for inhibiting unwanted activation of a *hedgehog-patched* pathway in an animal, comprising topically administering to the animal a composition comprising a purified hedgehog antagonist in a sufficient amount to reduce the unwanted activation of the *hedgehog-patched* pathway in a cell of the animal, wherein the hedgehog antagonist is an organic molecule having a molecular weight less than 750 amu and which binds to *smoothened* and lessens the severity of a *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function phenotype.

28. (New) A method for inhibiting unwanted activation of a *hedgehog-patched* pathway in an animal, comprising topically administering to the animal a composition comprising a purified hedgehog antagonist, or prodrug form thereof which is converted to a hedgehog antagonist under physiological conditions of the host animal, in a sufficient amount to reduce the unwanted activation of the *hedgehog-patched* pathway in a cell of the animal, wherein the hedgehog antagonist is an organic molecule which interacts with *smoothened* or a complex comprising *smoothened* and lessens the severity of a *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function phenotype.

29. (New) A method for inhibiting unwanted hair growth in an animal, comprising administering to the animal a composition comprising a purified hedgehog antagonist in a sufficient amount to inhibit activation of a *hedgehog-patched* pathway of a cell in the animal and thereby inhibit hair growth, wherein the hedgehog antagonist is an organic molecule having a molecular weight less than 750 amu and which binds to *smoothened* and lessens the severity of a phenotype of *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function.

30. (New) A method for inhibiting unwanted hair growth in an animal, comprising contacting a cell sensitive to the hedgehog protein with a composition comprising a purified hedgehog antagonist, or prodrug form thereof, in a sufficient amount to inhibit activation of a *hedgehog-patched* pathway of a cell in the animal to the hedgehog protein and thereby inhibit hair growth, wherein the hedgehog antagonist is a organic molecule having a molecular weight less than 750 amu and which interacts with *smoothened* or a complex comprising *smoothened* and lessens the severity of a phenotype of *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function.

31. (New) A method for inhibiting unwanted cell proliferation, comprising contacting a cell having a phenotype of *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function with a composition comprising a hedgehog antagonist in a sufficient amount to inhibit activation of a *hedgehog-patched* pathway of the cell and thereby inhibit unwanted proliferation of the cell, wherein the hedgehog antagonist binds to *smoothened* and lessens the severity of a phenotype of *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function.

32. (New) A method for inhibiting unwanted cell proliferation, comprising contacting a cell having a phenotype of *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function with a composition comprising a hedgehog antagonist, or prodrug form thereof, in a sufficient amount to inhibit activation of a *hedgehog-patched* pathway of the cell and thereby inhibit unwanted proliferation of the cell, wherein the hedgehog antagonist interacts with *smoothened* or a complex comprising *smoothened* and lessens the severity of a phenotype of *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothened* gain-of-function.

33. (New) The method of claim 31 or 32, wherein the composition comprises a purified hedgehog antagonist.

34. (New) The method of claim 31 or 32, wherein inhibiting unwanted cell proliferation comprises treating basal cell carcinoma.

35. (New) The method of claim 31 or 32, wherein inhibiting unwanted cell proliferation comprises treating medulloblastoma.

Sub
CS
By
36. (New) A method for inhibiting unwanted activation of a *hedgehog-patched* pathway in an animal, comprising
providing a cell,
treating the cell with a test compound, wherein the test compound is an organic molecule having a molecular weight less than 750 amu,
detecting a decrease in the level of activation of a *hedgehog-patched* pathway in the cell indicative of a *hedgehog* inhibitory activity of the test compound, and
administering to the animal a composition comprising the test compound having a *hedgehog* inhibitory activity in an amount sufficient to reduce the activation of a *hedgehog-patched* pathway in a cell of the patient.

37. (New) A method for preparing a pharmaceutical preparation, comprising
providing a cell,
treating the cell with a test compound, wherein the test compound is an organic molecule having a molecular weight less than 750 amu,
detecting a decrease in the level of activation of a *hedgehog-patched* pathway in the cell indicative of a *hedgehog* inhibitory activity of the test compound, and
formulating a pharmaceutical preparation by combining the test compound having a *hedgehog* inhibitory activity with a pharmaceutically acceptable excipient.

The claims presented above incorporate changes as indicated by the marked-up versions below.

1. (Amended) A method for inhibiting [paracrine and/or autocrine signals produced by a hedgehog proteins] unwanted activation of a *hedgehog-patched* pathway in an animal, comprising [contacting a cell sensitive to the hedgehog protein with a hedgehog antagonist in a sufficient amount to reduce the sensitivity of the cell to the hedgehog protein, wherein the hedgehog antagonist is a] administering to the animal a composition comprising a purified organic molecule having a [molecule] molecular weight less than 750 amu in an amount sufficient to reduce the activation of the *hedgehog-patched* pathway in a cell, wherein the organic molecule binds to *smoothed* and lessens the severity of a *hedgehog* gain-of-function, *patched* loss-of-function, or *smoothed* gain-of-function phenotype.
2. (Amended) A method for inhibiting an altered growth state of a cell having a *ptc* loss-of-function phenotype or a *smoothed* gain-of-function phenotype, comprising contacting the cell with a [*ptc* agonist] composition in a sufficient amount to inhibit the altered growth state, wherein the [*ptc* agonist is] composition comprises a purified organic molecule having a [molecule] molecular weight less than 750 amu and which interacts with *smoothed* or a complex comprising *smoothed* and inhibits aberrant signal transduction resulting from a *patched* loss-of-function or *smoothed* gain-of-function phenotype.
15. (Amended) The method of any of claims 1-3 [10], wherein the [hedgehog antagonist] organic molecule inhibits hedgehog-mediated signal transduction with an ED₅₀ of 1 mM or less.
16. (Amended) The method of any of claims 1-3 [10], wherein the [hedgehog antagonist] organic molecule inhibits hedgehog-mediated signal transduction with an ED₅₀ of 1 μM or less.
17. (Amended) The method of any of claims 1-3 [10], wherein the [steroidal alkaloid] organic molecule inhibits hedgehog-mediated signal transduction with an ED₅₀ of 1 nM or less.
18. (Amended) The method of claim[s 1 or] 2, wherein the cell is contacted with the [hedgehog antagonist] organic molecule *in vitro*.